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Case Report

Rifampicin-Induced Circulatory Shock Following Re-Exposure During Latent Tuberculosis Therapy: A Case Report

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Abstract

Background: Rifampicin is a cornerstone agent in the management of active and latent tuberculosis infection and is generally well tolerated. Severe systemic reactions, including circulatory shock, are rare and most commonly reported following intermittent dosing or drug re-exposure. The clinical presentation may closely mimic septic shock, posing significant diagnostic challenges.
Case Presentation: A 29-year-old male receiving rifampicin 600 mg daily for latent tuberculosis infection developed acute fever, gastrointestinal symptoms, and profound hypotension within two hours of drug re-exposure after a three-week interruption. On presentation, blood pressure was 78/46 mmHg with tachycardia (128 beats/min) and elevated serum lactate (4.8 mmol/L), necessitating vasopressor support. Inflammatory markers were modestly elevated (CRP 6.5 mg/L, procalcitonin 0.18 ng/mL), serum tryptase was normal, and microbiological cultures remained negative. Hemodynamic stabilization occurred within 24 hours following supportive care and permanent discontinuation of rifampicin. Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a score of 9, consistent with a definite adverse drug reaction.
Conclusion: Rifampicin-induced shock is an uncommon but potentially life-threatening complication that may occur following drug re-exposure and can clinically resemble septic shock. Recognition depends on careful attention to temporal relationships, exclusion of infection, and early withdrawal of the offending agent. Clinician awareness is essential, particularly in tuberculosis-endemic settings where rifampicin use is widespread.

Keywords: *Rifampicin-induced shock, Latent tuberculosis infection, Drug re-exposure, Circulatory shock, Adverse drug reaction*

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Introduction

Rifampicin remains a cornerstone in the treatment of both active tuberculosis and latent tuberculosis infection, owing to its potent bactericidal activity, sterilizing capacity, and favorable impact on treatment outcomes.[1] It is generally well tolerated, with commonly reported adverse effects including gastrointestinal intolerance, hepatotoxicity, and mild flu-like reactions.[2,3] Severe hypersensitivity reactions are uncommon and are therefore not routinely anticipated in standard clinical practice.[4]

Among these rare events, rifampicin-induced shock represents an exceptionally uncommon but potentially life-threatening adverse drug reaction. The majority of reported cases have occurred in the context of intermittent dosing schedules or following drug re-exposure after a period of interruption, suggesting an immunologically mediated mechanism.[5] Clinical presentation is typically abrupt, characterized by fever, gastrointestinal symptoms, hypotension, and hemodynamic instability, often closely mimicking septic shock. This overlap in presentation poses a significant diagnostic challenge, particularly in acute care settings where sepsis is appropriately prioritized.

In tuberculosis-endemic regions, where rifampicin is widely prescribed across diverse clinical scenarios, including prophylaxis prior to immunomodulatory therapy, the ability to recognize rare but severe drug reactions assumes particular importance. Failure to identify rifampicin-induced shock may lead to unnecessary antimicrobial escalation, invasive investigations, and inadvertent re-challenge, potentially resulting in more severe reactions.

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This report is a case of acute circulatory shock occurring shortly after rifampicin re-exposure in a patient receiving treatment for latent tuberculosis infection. Through this case, the authors try to highlight the characteristic clinical pattern, diagnostic pitfalls, proposed pathophysiological mechanisms, and management considerations associated with this rare but clinically significant adverse reaction.

Case Presentation

A 29-year-old male with **no known medical comorbidities** was evaluated for treatment of latent tuberculosis infection prior to initiation of anti–tumor necrosis factor therapy for inflammatory arthritis. He had **no prior history of tuberculosis disease**, drug allergies, atopy, or previous hypersensitivity reactions. Baseline physical examination was unremarkable. Initial laboratory investigations revealed hemoglobin 14.2 g/dL, total leukocyte count 6,800/mm³, platelet count 2.4 × 10^5/mm³, serum creatinine 0.9 mg/dL, AST 28 U/L, ALT 32 U/L, total bilirubin 0.8 mg/dL, and C-reactive protein (CRP) 2.1 mg/L.

The patient was **initiated on rifampicin 600 mg** once daily for latent tuberculosis infection. After 10 days of therapy, he reported mild nausea and epigastric discomfort without fever, rash, hemodynamic instability, or systemic symptoms. Liver enzymes remained within normal limits. Rifampicin was discontinued due to gastrointestinal intolerance. The patient remained asymptomatic during a subsequent three-week drug-free interval.

Following clinical reassessment, rifampicin 600 mg once daily was reintroduced as monotherapy. Approximately 90 minutes after ingestion of the first re-exposure dose, the patient developed acute nausea, abdominal cramping, and generalized malaise. Within two hours, he experienced high-grade fever (measured at home as 38.9°C) and multiple episodes of vomiting. Over the next hour, he developed progressive dizziness and near-syncope. Blood pressure measured at home was approximately 80/50 mmHg, prompting urgent presentation to the emergency department approximately four hours after drug ingestion.

On arrival, the patient was febrile (39.1°C), hypotensive with a blood pressure of 78/46 mmHg, tachycardic at 128 beats per minute, and tachypneic at 24 breaths per minute. Oxygen saturation was 98% on room air. He was alert but appeared pale and diaphoretic. There was no urticaria, angioedema, flushing, bronchospasm, or stridor. Cardiovascular and respiratory examinations were otherwise unremarkable, and no focal source of infection was identified on systemic examination.

Initial laboratory evaluation demonstrated hemoglobin 13.9 g/dL, leukocyte count 9,200/mm³ with 78% neutrophils, and platelet count 2.1 × 10^5/mm³. Serum lactate was elevated at 4.8 mmol/L. Serum creatinine had risen to 1.3 mg/dL from a baseline of 0.9 mg/dL. AST and ALT were mildly elevated at 42 U/L and 47 U/L, respectively. CRP was 6.5 mg/L, and procalcitonin measured 0.18 ng/mL. Arterial blood gas analysis revealed metabolic acidosis with a pH of 7.31 and bicarbonate of 18 mmol/L. Serum tryptase obtained within four hours of symptom onset was 5.4 ng/mL (reference <11.4 ng/mL).

The patient received two liters of intravenous crystalloid within the first hour of resuscitation. Empiric broad-spectrum antimicrobial therapy with piperacillin–tazobactam was initiated due to concern for septic shock. Despite adequate fluid resuscitation, hypotension persisted, necessitating initiation of norepinephrine infusion at 0.08 µg/kg/min. Blood and urine cultures were obtained prior to antibiotic administration. Imaging studies did not identify an infectious source.

Over the next 12 hours, the patient demonstrated gradual hemodynamic improvement. Serum lactate decreased to 1.9 mmol/L at 18 hours, and vasopressor support was discontinued at 20 hours. Blood and urine cultures remained negative at 48 hours. Inflammatory markers did not demonstrate progressive elevation. Given the close temporal relationship between rifampicin ingestion and symptom onset, the absence of an identifiable infectious source, low procalcitonin level, normal serum tryptase, and rapid clinical improvement following discontinuation of rifampicin, a diagnosis of rifampicin-induced shock was established.

Rifampicin was permanently discontinued, and antibiotics were stopped after 48 hours once sepsis was reasonably excluded. Renal function and liver enzymes normalized within 72 hours. The patient remained clinically stable and was discharged on hospital day four. Subsequent multidisciplinary consultation was undertaken to determine alternative strategies for latent tuberculosis management prior to immunomodulatory therapy. Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a score of 9, consistent with a definite adverse drug reaction. The rapid onset of symptoms within two hours of re-exposure, absence of alternative etiologies, and prompt resolution following drug withdrawal strongly supported rifampicin as the precipitating agent.

Table 1. Hemodynamic and Laboratory Parameters Over Time

Parameter	Baseline (Pre-treatment)	At Presentation (4 h post-dose)	18 Hours	72 Hours
Temperature (°C)	36.8	39.1	37.4	36.9
Blood Pressure (mmHg)	122/78	78/46	104/64	118/76
Heart Rate (beats/min)	74	128	92	76
Serum Lactate (mmol/L)	–	4.8	1.9	1.2
Hemoglobin (g/dL)	14.2	13.9	13.7	14.0
Total Leukocyte Count (/mm³)	6,800	9,200	8,100	7,200
Platelets (×10^5/mm³)	2.4	2.1	2.2	2.3
Creatinine (mg/dL)	0.9	1.3	1.1	0.9
AST (U/L)	28	42	38	30
ALT (U/L)	32	47	40	33
CRP (mg/L)	2.1	6.5	5.2	2.4
Procalcitonin (ng/mL)	–	0.18	0.12	0.08

Discussion

This case illustrates a rare but clinically consequential adverse reaction to rifampicin characterized by abrupt circulatory collapse shortly after drug re-exposure. Although rifampicin is widely regarded as safe and remains foundational to tuberculosis management, severe systemic reactions continue to be described, most commonly in the setting of interrupted therapy followed by re-administration. The temporal precision observed in this case, symptom onset within two hours of ingestion, strongly supports a causative relationship and aligns with previously reported patterns of rapid systemic involvement.[5,6]

One of the most challenging aspects of rifampicin-induced shock is its striking resemblance to septic shock.[6,7] Fever, hypotension, tachycardia, metabolic acidosis, and elevated lactate appropriately trigger sepsis protocols in acute care settings. In this patient, initial management as presumed septic shock was both clinically appropriate and unavoidable. However, several features warrant attention when reconsidering the diagnosis: the immediate temporal relationship to drug intake, lack of an identifiable infectious source, relatively modest inflammatory marker elevation, low procalcitonin, and rapid hemodynamic recovery following discontinuation of the suspected agent. Together, these findings suggest a systemic inflammatory process that mimics infection without microbial etiology.

The pathophysiology of rifampicin-induced shock remains incompletely understood and is likely heterogeneous. Classical IgE-mediated anaphylaxis does not fully explain many reported cases, particularly those without urticaria, bronchospasm, or elevated serum tryptase. In the present case, normal tryptase levels and absence of cutaneous or respiratory manifestations argue against a typical mast cell–driven reaction. Alternative mechanisms have been proposed, including immune complex formation during re-exposure, complement activation, cytokine release, and nitric oxide–mediated vasodilation. It is plausible that initial exposure results in immunologic priming, while subsequent dosing triggers a systemic inflammatory cascade sufficient to produce distributive shock without classical allergic features. This spectrum concept, rather than a single mechanistic pathway, may better account for the variability observed across published cases.

Re-exposure appears to be a consistent risk factor.[8] Historical literature from intermittent rifampicin regimens described “flu-like syndrome” and severe systemic reactions occurring predominantly after treatment interruption.[2] Even when initial intolerance is mild and non-immunologic in nature, immune sensitization may still occur. The absence of severe symptoms during first exposure should therefore not be interpreted as reassurance against future reactions. This case reinforces the need for caution when restarting rifampicin after a drug-free interval, particularly in non-emergent settings such as latent tuberculosis therapy.

From a diagnostic standpoint, the distinction between septic and drug-induced shock hinges less on initial presentation and more on pattern recognition over time. Early management should prioritize stabilization; however, clinicians should revisit the differential diagnosis when cultures remain negative, inflammatory biomarkers are discordant with clinical severity, and improvement occurs rapidly after withdrawal of a recently administered medication. Anchoring bias toward infection in febrile hypotensive patients is understandable but may obscure less common etiologies. In tuberculosis-endemic regions, where rifampicin use is widespread and sepsis prevalence is high, maintaining diagnostic flexibility becomes especially important.

Management remains largely supportive. Prompt discontinuation of rifampicin and aggressive hemodynamic stabilization are central. The role of corticosteroids is unclear and inconsistently reported in the literature. Desensitization strategies have been attempted in selected cases, but evidence supporting their safety following severe shock is limited. Given the potential for recurrence and possibly greater severity upon re-challenge, most authors recommend permanent avoidance after significant systemic reactions. In patients requiring ongoing tuberculosis prophylaxis or treatment, alternative regimens must be individualized through multidisciplinary collaboration, balancing infectious risk with drug safety.

This case underscores an important clinical principle: common drugs can produce uncommon but dramatic reactions, particularly under conditions of re-exposure. Recognition depends not only on laboratory data but also on careful attention to chronology. In an era of protocol-driven acute care, the temporal relationship between drug administration and symptom onset remains one of the most powerful diagnostic tools available to clinicians.

In **conclusion**, rifampicin-induced shock is an uncommon but potentially life-threatening adverse reaction that most frequently occurs following drug re-exposure. Its clinical presentation often mimics septic shock, posing a diagnostic challenge in acute care settings. This case, supported by existing literature, underscores the importance of maintaining a high index of suspicion for drug-induced etiologies in patients presenting with acute circulatory collapse shortly after rifampicin administration. Prompt discontinuation of the offending agent and supportive care are central to management, while future rifampicin exposure should generally be avoided. Increased awareness of this entity is essential, particularly in tuberculosis-endemic settings, to ensure timely diagnosis, appropriate management, and informed therapeutic decision-making.

Declarations

Ethics Approval and Consent to Participate: Ethics committee approval was not required for this case report in accordance with institutional policy, as it describes a single patient without experimental intervention. The report was prepared in compliance with the principles of the Declaration of Helsinki.

Consent for Publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying clinical data. A copy of the signed consent form is available for review by the editorial office upon request.

Availability of Data and Materials: All relevant clinical data supporting the findings of this case are included within the article. No additional datasets were generated or analyzed.

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